CLAIMS

WHAT IS CLAIMED IS:

1. In a method of forming a complex between a probe containing probe nucleobases and a target containing target nucleobases, comprising mixing said probe and said target under hybridizing conditions, the improvement wherein at least one blocking agent comprising at least one nucleobase is conjugated to said probe and/or said target prior to hybridizing said probe with said target, wherein said conjugation enhances an avidity and/or a specificity of said hybridizing.

2. The method of claim 1, wherein said conjugation enhances said avidity and/or said specificity by hindering said probe and/or said target from existing in a conformation antithetical to said hybridization.

3. The method of claim 2, wherein said conformation is a hairpin structure.

4. The method of claim 1, wherein said at least one blocking agent contains up to five nucleobases.

5. The method of claim 1, wherein said at least one blocking agent contains up to two nucleobases.

6. The method of claim 1, wherein said at least one nucleobase is the only nucleobase contained in said at least one blocking agent.

7. The method of claim 6, wherein said at least one nucleobase is provided as a free nucleobase, in a nucleoside or in a nucleotide.

8. The method of claim 6, wherein said at least one blocking agent is a free nucleobase.

9. The method of claim 6, wherein prior to said mixing, an amount of said at least one blocking agent is conjugated to said probe and/or to said target.

10. The method of claim 9, wherein said at least one nucleobase is provided in a quantity that is 1-200% of a number of said probe nucleobases that are Watson-Crick complements to said at least one nucleobase.

11. The method of claim 10, wherein said quantity is about 25% of said number of said probe nucleobases that are Watson-Crick complements to said at least one nucleobase.

12. The method of claim 9, wherein said at least one nucleobase is provided in a quantity that is 1-200% of a number of said probe nucleobases that are identical to said at least one nucleobase.

13. The method of claim 12, wherein said quantity is about 100% of said number of said probe nucleobases that are identical to said at least one nucleobase.

14. The method of claim 9, wherein said at least one nucleobase is provided in a quantity that is 1-200% of a number of said target nucleobases that are Watson-Crick complements to said at least one nucleobase.

15. The method of claim 14, wherein said quantity is about 25% of said number of said target nucleobases that are Watson-Crick complements to said at least one nucleobase.

16. The method of claim 9, wherein said at least one nucleobase is provided in a quantity that is 1-200% of a number of said target nucleobases that are identical to said at least one nucleobase.

17. The method of claim 16, wherein said quantity is about 100% of said number of said target nucleobases that are identical to said at least one nucleobase.

18. The method of claim 1, wherein said probe nucleobases are arranged in a probe sequence of interspersed purines and pyrimidines, and said target nucleobases are arranged in a target sequence at least partially complementary to said probe sequence.

19. The method of claim 1, wherein said probe has a sugar phosphate backbone.

20. The method of claim 1, wherein a backbone of said probe is uncharged or positively charged.

21. The method of claim 1, wherein said target is single-stranded DNA or single-stranded RNA.

22. The method of claim 1, wherein said target is double-stranded DNA, double-stranded RNA or DNA:RNA.

23. The method of claim 1, wherein said at least one blocking agent is not conjugated to said target.

24. The method of claim 1, wherein said at least one blocking agent is not conjugated to said probe.

25. The method of claim 1, wherein said at least one blocking agent is a naturally-occurring nucleobase selected from said group consisting of A, T, C, G and U.

26. The method of claim 1, wherein said at least one blocking agent is a synthetic nucleobase analogue.

27. The method of claim 1, wherein said probe has a probe directionality parallel to a target strand directionality of said target.

28. The method of claim 1, wherein said probe has a probe directionality anti-parallel to a target strand directionality of said target.

29. The method of claim 1, further comprising detecting said complex.

30. The method of claim 29, wherein said complex is formed with at least one of said probe and said target bound to a substrate, surface or biochip.

31. The method of claim 29, wherein said complex is detected by a change in a signal associated with a label.

32. The method of claim 31, wherein said label is at least one member selected from the group consisting of a spin label, a fluorophore, a chromophore, a chemiluminescent agent, an electro-chemiluminescent agent, a radioisotope, an enzyme, a hapten, an antibody and a labeled antibody.

33. The method of claim 29, wherein said complex is detected by analyzing an electronic characteristic of said complex.

34. The method of claim 29, wherein said detecting is conducted in a test medium and under a varied condition, wherein said varied condition is a member selected from the group consisting of: (a) a change in nonaqueous components of said test medium, (b) a change in a pH of said test medium, (c) a change in a salt concentration of said test medium, (d) a change of an organic solvent content of said test medium, (e) a change in a formamide content of said test medium, (f) a change in a temperature of said test medium, (g) a change in chaotropic salt concentration in said test medium, (h) a change in an electric current, (i) a change in a number of photons in the test medium, and (j) a change in an electrical property of the test medium.

35. The method of claim 34, wherein a laser beam is applied to said test medium to effect said change in the number of photons.

36. The method of claim 34, wherein said electrical property is electrical conductance.

37. The method of claim 34, wherein said electrical property is Q, a resonant structure of a transmission line or changes in phase or amplitude of a signal propagated in said transmission line in said test medium.

38. The method of claim 34, wherein said complex is detected under serially varied conditions.

39. The method of claim 31, wherein said label is added free in solution to said test medium.

40. The method of claim 29, further comprising:

(a) detecting a signal from a label, wherein said signal is correlated to a binding affinity between said probe and said target;

(b) varying a condition of a test medium;

(c) detecting a subsequent signal; and

(d) comparing said signal and said subsequent signal.

41. The method of claim 29, wherein said target is quantitated.

42. The method of claim 29, wherein an extent of complementarity between said probe and said target is detected.

43. The method of claim 1, wherein formation of said complex is facilitated by at least one intercalator.

44. The method of claim 1, wherein: (a) said complex is formed in a presence of at least one other probe containing a sequence of nucleobases complementary to a secondary target sequence different from a primary target sequence of said target; (b) said other probe differs from said probe by only a single nucleobase; (c) said other probe forms a complex with said target; and (d) said target is detected.

45. The method of claim 1, wherein the probe and the target hybridize in accordance with a Watson-Crick motif to form duplex, triplex or quadruplex nucleic acid complexes.

46. The method of claim 1, wherein the probe and the target hybridize in accordance with a homologous binding motif to form duplex, triplex or quadruplex nucleic acid complexes.

47. The method of claim 1, wherein said hybridizing is conducted in a homogeneous medium.